STATUS OF CLAIMS

Claims 1-41 are pending in the application. Claims 23-39 were previously withdrawn from consideration pursuant to a restriction requirement. Thus, claims 1-22 and 40-41 are currently under examination. Applicant has amended independent claim 1 to correct a minor typographical error. There is no issue of new matter.

REMARKS

Withdrawal of Rejection under 35 USC § 103(a) over Michal et al. and Sogo et al.

Applicants acknowledge with thanks the rejection of claims 1-22 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Pat. No. 6,287,285 (Michal et al.) in combination with the article, Sogo et al., "S-Nitrosothiols cause prolonged, nitric oxide mediated relaxation in human saphenous vein and internal mammary artery: therapeutic potential in bypass surgery" (Sogo et al.)

Rejection under 35 USC § 103(a) over Stamler et al. and Sogo et al.

Claims 1-22, 40 and 41 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Pat. No. 6,087,479 (Stamler et al.) in combination with the article, "S-Nitrosothiols cause prolonged, nitric oxide mediated relaxation in human saphenous vein and internal mammary artery: therapeutic potential in bypass surgery" (Sogo et al).

In response, Applicants respectfully traverse this rejection and its accompanying remarks. The prior art references, in combination, fail to teach or suggest *all* of the claim limitations. In addition, the teaching or suggestion to make the claimed combination and the reasonable expectation of success are not both found in the prior art, but rather, upon Examiner's own assumptions. This is contrary to the legal requirements set forth in *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) requiring that the teaching or suggestion and the reasonable expectation of success be found in the prior art and not the applicant's disclosures.

Claim 1 provides for a medical article comprising a first polymer matrix having a first nitric oxide donor compound disposed within the first polymer matrix and a second polymer matrix having a second nitric oxide donor compound disposed within the second

polymer matrix. The second nitric oxide donor compound differs from the first nitric oxide donor compound, and the first polymer matrix is chemically distinct from the second polymer matrix. The medical article is adapted, after placement at a delivery position on or within the body of a patient, for local delivery of the first nitric oxide donor compound and a nitric oxide product of the first nitric oxide donor compound and for local delivery of the second nitric oxide donor compound and a nitric oxide product of the second nitric oxide donor compound.

The claimed invention is structurally different from the device of Stamler et al. Stamler et al. does not teach a device having a first polymer matrix and a second polymer matrix each containing a nitric oxide donor compound, much less each containing different nitric oxide donor compounds. Sogo et al. does not remedy this deficiency and merely provides experimental data on various S-nitrosothiol compounds.

More specifically, citing col. 9 of Stamler et al., the Examiner urges that the "nitric oxide adduct can be incorporated into synthetic or natural matrix which is then used to coat those same contact surfaces of the device [which include a nitric oxide adduct]." However, this was not found to be the case. For example, col. 9, lines 48-64 read as follows (emphasis added):

> As mentioned above, the medical device or instrument may be made, such that at least in those portions of it which come into contact with blood, blood components or products, or vascular tissue, include a nitric oxide adduct. The nitric oxide adduct ***can directly or indirectly be linked to*** a synthetic material from which all or a portion of the device is formed….
>
> ***In another embodiment*** mentioned above, the nitric oxide adduct ***can be incorporated into a*** natural or synthetic ***matrix*** which is then used to coat those same contact surfaces of the device [i.e., those portions of the device which come into contact with blood, blood components or products, or vascular tissue]. The matrix can be a liquid into which the nitric oxide adduct has been mixed, which is then coated onto the contact surfaces of the medical device or instrument and then allowed to "set", dry, polymerize or otherwise become solid or semisolid….

Thus the portion of Stamler et al. cited by the Examiner is merely an expansion on various ***alternative*** strategies described in Stamler et al.. For example, see the Stamler et al. throughout, including the Abstract which states (emphasis added):

> The nitric oxide adduct can be present in a matrix coating on a surface of the medical device; can be coated per se on a surface of the medical device; can be directly or indirectly bound to reactive sites on a surface of the medical device; ***or*** at least a portion of the medical device can be formed of a material, such as a polymer, which includes the nitric oxide adduct."

Nowhere in Stamler et al. is it taught or suggested to employ first and second chemically distinct polymer matrices, *each having a nitric oxide donor disposed therein*, much less a first polymer matrix having a first nitric oxide donor disposed therein and a second polymer matrix having a second nitric oxide donor disposed therein that differs from the first nitric oxide donor.

The secondary reference, Sogo et al. does not remedy these deficiencies in Stamler et al. Specifically, Sogo et al. does not teach or suggest first and second chemically distinct polymer matrices, each having a nitric oxide donor disposed therein. Nor does Sogo et al. teach or suggest the use of first and second nitric oxide donors that differ from one another in a single device.

In particular, Sogo et al. describes four NO donor drugs: (1) N-(S-nitroso-N-acetylpenicillamine)-2-amino-2-deoxy-1,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose (RIG200), (2) S-nitrosoglutathione (GSNO), (3) glyceryl trinitrate (GTN) and (4) sodium nitroprusside (SNP). However, although Sogo et al. may refer to "RIG200 and GSNO" collectively as "S-nitrothiols" (see, e.g., p. 1237 left column, p. 1241, right column, etc.), nowhere in Sogo et al. is it taught or suggested that these drugs may be used in the same device, much less in the same device in two chemically distinct polymer matrices. (Similarly, Sogo et al. refers to "GTN and SNP" collectively as "NO donor drugs" but does not teach or suggest that these drugs may be used in the same device.)

In this regard, see also, for example, "Experimental protocol," p. 1237, which states (emphasis added): "Concentration-relaxation relationships were established in SV and IMA rings … Each ring was randomly allocated to treatment with increasing concentrations (0.01–10 μM) of ***either*** RIG200, GSNO, SNP ***or*** GTN in organ baths…"

Thus, nowhere in Sogo et al. is a combination of NO donor compounds described. Rather, Sogo et al. presents nitrosoglutathione and N-(S-nitroso-N-acetylpenicillamine) as *alternatives*, rather than *as a combination*.[1]

The addition of the disclosure of Sogo et al. to that of Stamler et al. on its face relies upon the use of undue hindsight, which is prohibited. *See Akso N.V. v. U.S. International Trade Commission*, 808 F.2d 1241, 1480-81, 1 U.S.P.Q.2d, 1241, 1246 (Fed. Cir. 1986), *cert. denied,* 482 U.S. 909 (1987), *Loctite Corp. v. Ultraseal Ltd.*, 781 F.2d 861, 874, 228 U.S.P.Q. 90-99 (Fed. Cir. 1985). Also see MPEP § 2142, second paragraph. The combination is based upon *applicant's own disclosure*, rather than the teachings within the four corners of Sogo et al. and Stamler et al.

The courts have been clear that there must be some *articulated reasoning with some rational underpinning* to support the legal conclusion of obviousness. *In re Kahn,* 441 F.3d 977, 988 (Fed. Cir. 2006), *cited with approval in, KSR Int'l v. Teleflex, Inc.*, 127 S. Ct. 1727, 1740-41, 82 USPQ 1385, 1396 (2007). Applicants state that the Examiner has not provided a rational underpinning to support the combination of two different NO donor compounds in two matrices.

In light of the above remarks, reconsideration and withdrawal of this rejection of the claims under 35 U.S.C. § 103 is respectfully requested.

[1] In addition to the preceding evidence, see further the experimental results in Sogo et al., in which response curves for RIG200 (N-(S-nitroso-N-acetylpenicillamine) are *separate and distinct* from response curves for GSNO (nitrosoglutathione) and there are no data or textual support for a combination of two or more NO donor compounds. (*See* Figures 3, 4, 5, 6, and their accompanying text.)

CONCLUSION

Applicants respectfully submit that all pending claims are in condition for allowance, early notification of which is earnestly solicited. Should the Examiner be of the view that an interview would expedite the application at large, request is made that the Examiner telephone the undersigned attorney at (703) 433-0510 in order to resolve any outstanding issues.

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Respectfully submitted,

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